



**BlueCross BlueShield  
Association**

An Association of Independent  
Blue Cross and Blue Shield Plans

August 20, 2004

Food and Drug Administration  
Division of Dockets Management  
5630 Fishers Lane  
Room 1061  
Rockville, MD 20852

**Allan M. Korn, M.D. FACP**  
Senior Vice President  
Clinical Affairs  
Chief Medical Officer

225 North Michigan Avenue  
Chicago, Illinois 60601-7680  
312.297.6840  
Fax 312.297.5726  
allan.korn@bcbsa.com

Docket #2004S-0233

The Blue Cross and Blue Shield Association (BCBSA) is pleased to respond to the "Solicitation of Comments on Stimulating Innovation in Medical Technologies" published in the Federal Register on May 24, 2004 (**Federal Register** Vol. 69, No. 100). BCBSA is an association of 41 independent Blue Cross and Blue Shield Plans ("Plans") providing health benefits to almost 92 million members, one in three Americans. BCBSA also provides scientific information on new technologies through BCBSA's Technology Evaluation Center (TEC), jointly operated with Kaiser Permanente. Technology assessments developed by TEC are available to all users on the web at <http://www.bcbs.com/tec/index.html>. TEC is also an AHRQ Evidence-based Practice Center.

HHS has expressed the concern in the solicitation that "new discoveries in basic sciences are not rapidly translating into new medical products for patients." A statistic is cited indicating that only one in five products that reach the clinical testing stage ever make it to marketing. There are two processes that limit the transformation of scientific discovery into clinical products that benefit patients. The first is the transfer of basic research from the laboratory to product development and testing in clinical trials. The second is the adoption of the outcomes of clinical trials into mainstream clinical practice. A key barrier to diffusion of effective new technologies is the dearth of quality information that can be used by decision-makers- physicians, payers, health plans, and consumers- "to make well-informed decisions regarding alternative strategies for diagnosis and treatment of common clinical conditions."<sup>1</sup> We agree that "the current clinical research enterprise in the United States is not consistently producing an adequate supply of information to meet the needs" <sup>2</sup> of decision-makers.

BCBSA is not in a position to comment on the research and development processes of private industry. It is clear, however, that truly innovative devices or priority new

---

<sup>1</sup> Sean R. Tunis, MD, et.al., "Practical Clinical Trials" JAMA, September 24, 2003, vol. 290, no.12, p. 1631.

<sup>2</sup> *Ibid.*, p. 1625

2004S-0233

C7

molecular entities have comprised only a small proportion of new products entering the FDA review cycle in recent years. One study found that 50% of all new drug approvals in the period 1995-2000 were for incrementally modified drugs while priority new molecular entities accounted for only 13% of NDAs.<sup>3</sup> Most new devices reviewed by the FDA are cleared for marketing based on their similarity, or substantial equivalence, to previously approved devices. These devices are not viewed as significant innovations and the FDA does not require evaluation of their clinical effectiveness.

In recent years, FDA has taken action to accelerate its review processes. Speedier FDA approvals have been achieved by postponing the collection and review of necessary data to the post-marketing period. Regrettably, the promise of post-marketing studies has often failed to produce good data on effectiveness necessary to determine the appropriate use of new technologies. Reliance on post-marketing studies or registries to fill in gaps in evidence has proven disappointing. In most instances, the promised data have not been forthcoming. Carticel is one example of this phenomenon. As a condition of Carticel's accelerated Biologics License Application (BLA) approval, Genzyme was required to conduct randomized trials to confirm clinical efficacy in the post-marketing setting. These trials were never completed, and the manufacturer claimed that patients were unwilling to enroll and investigators were unwilling to participate. As a result, FDA revised Carticel's label claim to second line use only, and this limited use and coverage of the product in clinical practice.

In evaluating new technologies for coverage consideration, health plans and employers seek evidence that the new technology improves clinical outcomes for patients or will otherwise have a positive impact on clinical management. Many of the new products in clinical testing may fail to reach the market because they are not shown to improve health outcome for patients. If such technologies do come to market, payers who require evidence of clinical value in order to provide coverage will deny coverage. What can the agencies of HHS, including AHRQ, do to improve this situation?

- The thresholds of evidence necessary to achieve FDA approval and coverage by Medicare should be defined clearly and communicated to developers of new technologies early in the development process. Clinical trials to demonstrate effectiveness should be designed to establish whether or not the evidence threshold is met. The evidence threshold for approval for marketing has not been the same as the threshold for coverage. The FDA seeks to determine that new drugs are safe and effective compared to placebo. Most devices are not required to demonstrate effectiveness at all. Payers must compare new technologies to alternative technologies and interventions. It is not in the interest of the beneficiary or society in general to have Medicare pay for technologies that are less effective than other products or modalities targeting the same clinical condition. Consideration should be given to raising the evidence threshold for FDA review.

- Premature approval and diffusion of new technologies before clinical value is established can actually stifle meaningful innovation. An example from the last decade was high dose chemotherapy with autologous stem cell or bone marrow transplant support for breast cancer. Many oncologists promoted this technology as being a break-through for advanced and high risk disease. Had this treatment entered the mainstream as standard practice, thousands of women would have received a toxic therapy that was no more effective than conventional treatment with greater risk of side effects and death. Erroneous acceptance of this treatment as standard treatment would have reduced the impetus, and perhaps research funding, to discover alternate break-through treatment approaches that may improve length and quality of life.
- Innovative break-through technologies must be evaluated in well-designed clinical trials that account for bias and that measure impact on the net health outcome. These trials can be costly to conduct. Contingent coverage for patient care costs in potentially definitive trials by Medicare may be appropriate in some instances. However, government support of the development and testing of new technologies should give government some voice in the ultimate marketing of the new technology. The phenomenon of huge price increases for drugs developed with government funding is troubling and should be addressed.
- Nongovernmental stakeholders, such as private employers and health plans, can promote rational technology development and diffusion through a greater focus on evidence-based clinical utility. Equitable funding mechanisms for high priority trials of clinical effectiveness should be put in place.

BCBSA and member Plans recognize that continued innovation in medical technology is essential if Americans are to continue having access to the clinical breakthroughs they have come to expect. Government agencies can play an important role in supporting innovation by clarifying expectations for demonstration of effectiveness and clinical benefit and by supporting the well-designed trials necessary to meet these expectations.

Thank you for this opportunity to comment on this critical issue. If you have any questions, please feel free to contact me at 312.297.6840.

Sincerely,

A handwritten signature in black ink, appearing to read "AM Korn M.D.", written in a cursive, flowing style.

Allan M. Korn, M.D., FACP